Virginia Department of Health
Division of Disease Prevention, Tuberculosis Control Program
Updated Guidance for Serum Drug Levels

I. In a recent UVA/VDH study*, diabetes was found to be significantly associated with slow response in the study population. Diabetic slow responders were significantly more likely to have serum levels of rifampin below the expected range.

II. Based on these findings, the Virginia Department of Health, Division of Disease Prevention, Tuberculosis Control Program (DDP-tb) is implementing the following changes for obtaining therapeutic drug monitoring for diabetic clients undergoing treatment for tuberculosis.

a. Contact DDP-tb within 24 hours of a TB case/suspect with diabetes being identified and treatment initiated.
b. DDP-tb will issue a serum drug level authorization approval form for INH and rifampin levels to the local health district.
c. After the client has been on anti-tuberculosis treatment for 2 weeks or shortly thereafter, the serum drug level specimens should be collected and immediately sent to the Pharmacokinetics Laboratory in Gainesville, Florida for testing.
d. Once the results are received:
    i. If the results are within normal limits, no further follow-up is needed unless clinical issues are identified in the future.
    ii. If the results are below expected range on one or both of the drugs, adjust the medications <u>once</u> according to the guidelines published by the Virginia Department of Health.
    iii. If the results are below expected range, DDP-tb will issue an authorization for repeat serum drug levels to be drawn and sent 1 week following the drug dosage adjustment.
    iv. If repeat drug level results remain below expected range, the case should be reviewed with a DDP-tb clinical consultant for further recommendations.
e. If any diabetic is later determined to have a slow response to treatment, treatment failure or relapse, the case should be reviewed with a DDP-tb clinical consultant for further recommendations.

* In 2009 – 2010, a retrospective analysis was undertaken of TB clients who were labeled as slow responders to treatment. Of the clients included in the analysis, 42 met criteria for slow response to treatment and had therapeutic drug monitoring (TDM) as part of their follow-up evaluation to determine the cause of the slow response. At the time of TDM among clients meeting criteria for slow response, all had persistent TB related symptoms and of the 23 patients with initial smear positive sputum specimens, 17 (74%) remained smear positive. The major finding of the analysis was that the majority of clients undergoing treatment for pulmonary TB that met the criteria for slow response to therapy were found to have serum drug levels of rifampin and isoniazid below the expected range. Diabetes was a significant risk factor for slow response. *Heysell, SK, Moore, JL, Keller, SJ, Houpt, ER. Therapeutic drug monitoring among slow responders to tuberculosis therapy in a state control program. *Emerg Infect Dis* 2010;16:1546-53.